REMARKS

Claims 245-260 are pending in the above-referenced application. Claims 245, 252 and 255 have been amended to more distinctly claim that which Applicants regard as their invention and to advance prosecution. Claims 256 and 257 have been cancelled. Applicants reserve the right to file subsequent continuation and/or divisional applications on subject matter originally encompassed by claims 245, 252 and 255 and cancelled claims 256 and 257.Claim 261 has been added. The amended claims and claim 261 are supported by the specification. No new matter has been added.

Applicants will submit Formal Drawings and a Supplemental Information Disclosure Statement in a Supplemental Response. The typographical error in claim 249 has been corrected.

The Written Description Rejection

Claims 245-260 have been rejected under 35 U.S.C. 112, first paragraph. It is asserted that the instantly claimed compositions are considered to lack written description in the specification as filed for a representative number of species of any possible nucleic acid construct which when introduced into a cell codes for and expresses a non-native polymerase which is capable of producing more than one copy of a nucleic acid sequence from said construct and wherein said polymerase is expressed solely in a eukaryotic cell because the text of the specification as filed provides only general guidance, and not specific guidance, for the design and use of the claimed constructs. Specifically, the Office Action states:

> In the instant case, the constructs are nucleic acid constructs which when present in a cell produce a polymerase product as well as other possible products. The genus the involves production of a product in a cell. Not all cells are alike, and the environmental conditions alter drastically from use of cells in cell culture to use of cells in a whole organism which are intimately connected

> to other cells in a whole organism. Thus, the genus of cells in which the nucleic acid constructs are expressed is critical to understanding the genus of the claimed constructs since the claims have the function limitation that the nucleic acid construct in introduced into a cell and codes for and expresses a non-native polymerase. Additionally, to understand the breath of the claimed genus, one of skill in the art must consider the breath of the nucleic acid constructs claimed. Typically in the art, only a vector-type construct is capable of having the function of coding for and expressing a protein from the encoding nucleic acid gene sequence. Since nucleic acid constructs are composed of nucleic acids, having a defined sequence of bases, one of skill in the art would not readily envisage any such nucleic acid construct absent the nucleic acid sequence of said construct. Thus, the claimed genus is extremely broad since it is drawn to any possible nucleic acid construct expressing a polymerase in a cell. And since the specification as filed does not further provide the essential material of defining the common elements of nucleic acid sequence structure of any such nucleic acid composition, one of skill in the art does not have a clear vision of a representative number of specie of any such nucleic acid construct. The invention should be clearly defined in the specification as filed and essential material to the claimed invention (such as the nucleic acid sequences of the claimed nucleic acid constructs) can only be incorporated by reference to a patent publication (see MPEP 608.01 (p)(A)).

Applicants respectfully traverse the rejection. First, Applicants note that in order to advance prosecution, claims 245 and 255 have been amended. Claim 245 now recites that the construct comprises a nucleic acid sequence which encodes a non-eukaryotic polymerase and contains a non-native intron and which is expressed solely in a eukaryotic cell and is capable of producing more than one copy of a nucleic acid sequence from said construct when introduced into a eukaryotic cell; claim 255 now recites that the construct when introduced into a non-eukaryotic cell produces a **non-eukaryotic nucleic acid product** comprising a **non-native intron**, which when in a eukaryotic cell, said

intron is substantially removed during processing and wherein **said non-eukaryotic nucleic acid product would be toxic to a non-eukaryotic cell in the absence of said non-native intron.** Applicants further note that claim 261 is directed to a construct that when introduced into a non-eukaryotic cell produces a nucleic acid product comprising a non-native intron, wherein said product would be toxic to a non-eukaryotic cell in the absence of said non-native intron and wherein said intron is substantially removed during processing and said intron is in a coding sequence of said nucleic acid product.

It is Applicants' position that the pending claims are adequately described. First, Figures 27-31 and 47 clearly describe obtaining the construct used in the method of the present invention. Furthermore, The MPEP in section §2163 II.A.3. (a) states:

> An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole..... The description need only describe in detail that which is new or not conventional..... This is equally true whether the claimed invention is directed to a product or a process.

A specification may, within the meaning of 35 U.S.C. 112, first paragraph, contain a written description of a broadly claimed invention without describing all species that the claim encompasses. Furthermore, the following specific applications are described in the specification on pages 87-88:

a) Conditional inactivation of genes when these genes would be lethal to the host cell or when present in a host cells introduce a danger;

b) Expression of polymerases (e.g., T3, T7 and SP6) in compatible cells;

c) Cloning of incompatible genes together on the same construct, eg., a single construct containing sequences for the production of T7 promoter directed transcript(s) of choice and T7 RNA polymerase

Representative samples are not required by the statute and are not an end in themselves. *Amgen, Incorporated v. Chugai Pharmaceutical Company, Limited,* 18 USPQ2d 1016, 1027 (Fed. Cir. 1991). It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. *Ex parte Obukowicz,* 27 USPQ2d 1063 (BPAI 1993).

Furthermore, Applicants take issue with the assertion made in the Office Action that it is necessary to provide the nucleic acid sequence of the claimed constructs. This assertion is *contra* to the policies stated in the MPEP II.A.3.:

> Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. For example, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross-reactivity may be sufficient to show possession of the claimed invention to one of skill in the art.

Example 19 in the specification describes a particular polymerase, a method for picking sites for inserting an intron(s) into the polymerase and describes and exemplary intron that could be used. Any other polymerases of known sequence could have been used by carrying out the same steps as described in the example. Any other intron may have been used. The sequences are not a necessary parts of the invention. They were included as an example to teach how to create the constructs used in the present invention.

Clearly, the nucleic acid sequences of the constructs of the present invention and cells where the constructs are expressed are non-critical features of the invention and thus require no written support. A description need not be provided for features that are not essential or critical to the invention. *Ethicon Endo-Surgery, Inc. v. United States Surgical Corporation,*

*93 F. 3*d 1572 (Fed. Cir. 1996). An inventor need not explain every detail since he is speaking to those skilled in the art. What is conventional knowledge will be read into the disclosure. *In re Howarth*, 654 F.2d 103, 210 USPQ 689 (CCPA 1981).

In view of the above arguments, Applicants assert that the rejections under 35 U.S.C. 112, first paragraph has been overcome. Applicants therefore request that the rejection under 35 U.S.C. 112, first paragraph be withdrawn.

The Rejections Under 35 U.S.C. 102

Four rejections were made under 35 U.S.C. 102. Each will be discussed specifically below.

Wagner et al.

Claims 245-247 and 249-254 have been rejected under 35 U.S.C. 102(e) as being anticipated by Wagner et al., U.S. Patent No. 5,591,601. The Office Action specifically states with respect to Wagner:

> Wagner et al. taught in col. 2, line 46, through col. 3, line 2:
>
> The present invention is based, in part on Applicants' discovery of significant gene expression from a DNA construct complexed to T7 RNAP, which construct contains a T7 RNAP gene driven by a T7 promoter and another nucleotide sequence encoding a functional or reporter gene i.e. a gene of interest, under the control of a second T7 promoter (T7/T7 gene-construct). One unique feature of the construct which distinguishes this system from other gene expression systems is that both the initiation and maintenance of gene expression depend upon the binding of T7 RNAP to DNA prior to the introduction of the construct into host cells. The complex of prebound RNAP to plasmid DNA is stable without detachment during entry into cells. Once the DNA-RNAP enzyme complex enters the cytoplasm of the cells, transcription is initiated immediately by the plasmid. The

> subsequent production of T7 RNAP enzyme, in turn, triggers transcription of the functional/reporter gene as well as continued synthesis of additional T7 RNAP, thus it is both a self-initiating and self-sustaining system. The transcription of both the T7 RNAP and the functional/reporter genes can be driven repeatedly by newly synthesized T7 RNAP in the cell cytoplasm without nuclear integration.
>
> In col. 5, lines 8-9, they further teach that this system is used in eukaryotic cells. In col. 6, lines 65-67 and col. 7, lines 1-5, they teach that "[a]lso within the scope of the invention is the expression of oligo-ribonucleotide sequences, that include anti-sense RNA and ribozymes that function to inhibit the translation of a variety of mRNA. Anti-sense RNA acts to directly block the translation of mRNA by biding to targeted mRNA and preventing protein translation, either by inhibition of ribosome binding and/or translocation or by bringing about the nuclease degradation of the mRNA molecule itself."...

Applicants respectfully traverse the rejection. However, in order to advance prosecution, claim 245 has been amended to recite that the construct comprises **a nucleic acid sequence which encodes a non-eukaryotic polymerase and contains a non-native intron**, wherein said polymerase is expressed solely in a eukaryotic cell and said polymerase is capable of producing more than one copy of a nucleic acid sequence from said construct when introduced into a eukaryotic cell. Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Foundation v. Genentech Inc. 927 F. 2d 1565, 18 USPQ2d 1001, 18 USPQ2d 1896 (Fed. Cir. 1991).* The construct of Wagner is missing two elements of the construct of the present invention. It does not contain a non-native intron and Wagner also requires the presence of T7 RNA polymerase to be introduced into the cell.

The other claims, rejected, claims 246-247 and 249-254 depend from claim 245. Therefore, claims 246-247 and 249-254 are also not anticipated by Wagner et al.

In view of the amendments to claim 245 and the above arguments, Applicants assert that the rejection of claims 245-247 and 249-254 over Wagner et al. under 35 U.S.C. 102(e) have been overcome. Therefore, Applicants respectfully request that this rejection be withdrawn.

Fuerst et al.

Claim 245 has been rejected under 35 U.S.C. 102 (b) as being anticipated by Fuerst et al. (PNAS, Vol. 83, pp. 8122-8126, 1986). The Office Action specifically states:

> Fuerst et al. taught expression of a bacteriophage T7 RNA polymerase in eukaryotic human TK-143 and He La cells (see page 8122, col. 2, "virus and cells" and figure 1 on page 8123 for description of the recombinant virus with T7 polymerase used to infect the eukaryotic cells).

Applicants respectfully traverse the rejection. As noted above, amended claim 245 is directed to a construct comprising **a nucleic acid sequence which encodes a non-eukaryotic polymerase and contains a non-native intron**, wherein said polymerase is expressed solely in a eukaryotic cell and said **polymerase is capable of producing more than one copy of a nucleic acid sequence from said construct when introduced into a eukaryotic cell**. The system of Fuerst et al. is missing two elements of the construct of the present invention. It does not contain a non-native intron and secondly, Fuerst et al. does not use a single construct but is forced to use a two vector system.

In view of the amendments to claim 245 and the above arguments, Applicants assert that the rejection of claim 245 over Fuerst et al. under 35

U.S.C. 102(b) have been overcome. Therefore, Applicants respectfully request that this rejection be withdrawn.

DeYoung et al.

Claims 255-259 are rejected under 35 U.S. C. 102(b) as being anticipated by De Young et al. (Biochemistry, 1994, Vol. 33, No. 40, pp. 12127-12138). The Office Action specifically states:

> De Young et al. taught making plasmid constructs as in figure 3 (page 12129) having U1-ribozyme constructs expressed from a T7 promoter. They taught on page 12130, col.2, the expression of this construct in COS-1 cells. Since U1 introns are introns that are the same U1 introns used in the example in the instant specification, and since the ribozymes taught by De Young et al. are flanked by the U1 intron in the same manner as the U1 intron flanks the antisense in the examples in the instant specification, the U1 ribozyme constructs are considered to anticipate the instant claims.

Applicants respectfully traverse the rejection. As noted above, claim 255 has been amended to recite that the claimed construct when introduced into a non-eukaryotic cell produces a **non-eukaryotic nucleic acid product comprising a non-native intron,** which when in a eukaryotic cell, said intron is substantially removed during processing **and wherein said non-eukaryotic nucleic acid product would be toxic to a non-eukaryotic cell in the absence of said non-native intron**. In contrast, the construct of DeYoung **does not** produce a non-eukaryotic nucleic acid product containing a non-native intron which would be toxic to a non-eukaryotic cell in the absence of a non-native intron. The construct of DeYoung produces a ribozyme and only contains U1 sequences. Applicants wish to clarify that U1 sequences are not intron sequences.

Applicants note that claims 256-259 depend from claim 255. Therefore, claims 256-259 would also not be anticipated by DeYoung et al.

Clearly, DeYoung does not teach a vector containing all of the elements of the claimed constructs of the present invention. Therefore, claims 255-259 are not anticipated by DeYoung and the rejection of the claims under 35 U.S.C. §102(b) should be withdrawn.

Meyer, Jr. et al.

Claims 255 and 258-260 are rejected under 35 U.S.C. 102 (e) as being anticipated by Meyer, Jr. et al. (U.S. Patent 5,574,142). The Office Action specifically states:

> Meyer, Jr. et al. taught a covalently linked conjugate of an oligonucleotide (ODN) with a peptide and a carrier or targeting ligand, where the oligonucleotide is capable of binding to a target sequence of DNA, RNA or protein inside the target cell. The peptide is capable of being digested by proteolytic enzymes inside the target cell and is thus a processing element that is substantially removed during processing. (See abstract and Figure 2) In col. 1. Lines 16-34, they discuss where the ODN is an antisense oligonucleotide. In col. 2, lines 8-15, they discuss where ODN is a ribozyme. In col. 1, line 53, through col. 2 line 7, they discuss where the ODN binds a protein and wherein it binds HIV, and viral reverse transcriptase (required for viral replication). These ODNS are single stranded.

Applicants respectfully traverse the rejection. First, Applicants take issue with the assertion that proteolytic enzymes inside the target cell are actually processing elements. Second, as noted above, claim 255 has been amended to recite that the claimed construct when introduced into a non-eukaryotic cell produces a **non-eukaryotic nucleic acid product comprising a non-native intron,** which when in a eukaryotic cell, said intron is substantially removed during processing and wherein said non-eukaryotic nucleic acid product would be toxic to a non-eukaryotic cell in the absence of said non-native intron. Clearly, the entity of Meyer et al. does **not** produce a **non-eukaryotic** nucleic acid product that contains a non-native intron.

Claims 256-260 depend from claim 255. Therefore, claims 256-260 are also not anticipated by Meyer et al., Jr.

In view of the above arguments, Applicants assert that the rejections under Meyer et al., Jr. under 35 U.S.C. 102(e) have been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

Summary and Conclusions

Claims 245-260 are presented for further examination. Claims 245 and 255 have been amended. Claims 256-257 have been cancelled. Claim 261 has been added.

No fee or fees are believed due for this paper or the accompanying Petition. In the event that any fee or fees are due, however, The U.S. Patent and Trademark Office is hereby authorized to charge the amount of any such fee to Deposit Account 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Respectfully submitted,

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